

10/613,411

***** STN Columbus *****

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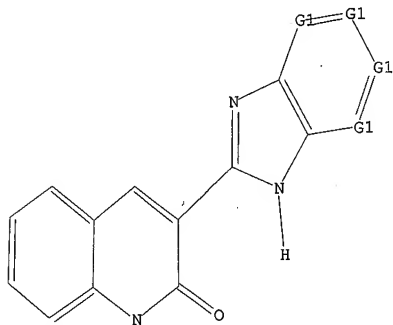
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L1 HAS NO ANSWERS

L1 STR



G1 C,N

Structure attributes must be viewed using STN Express query preparation.

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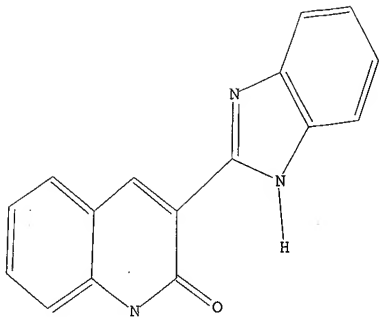
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L2 HAS NO ANSWERS

L2 STR

10/613,411



Structure attributes must be viewed using STN Express query preparation.

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L5 18 L3 NOT L4

=> file ca

=> s 15
L6 3 L5

=> d ibib abs fhitrn hitrn 1-3

L6 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 138:153534 CA

TITLE: Preparation of benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

INVENTOR(S): Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea, William R.; McBride, Christopher; Jazan, Elisa
Chiron Corporation, USA

PATENT ASSIGNEE(S): U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S.
SOURCE: Pat. Appl. 2002 107,392.

DOCUMENT TYPE: CODEN: USXXCO
LANGUAGE: Patent
FAMILY ACC. NUM. COUNT: 2 English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Patent

10/613,411

US 2003028018	A1	20030206	US 2002-116117	20020405
US 2002107392	A1	20020808	US 2001-951265	20010911
US 6605617	B2	20030812		
US 2003158224	A1	20030821	US 2002-284017	20021030
WO 2003087095	A1	20031023	WO 2003-US10463	20030404

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-232159P P 20000911
 US 2001-951265 A2 20010911
 US 2002-116117 A 20020405

OTHER SOURCE(S): MARPAT 138:153534
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO₂H, certain NH₂ derivs.; R₁-R₄ = H, halo, cyano, NO₂, OH or derivs., NH₂ or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO₂H and esters and amides; R₅-R₈ = H, halo, NO₂, OH or derivs., NH₂ or derivs., SH or derivs., cyano, etc.; R₉ = H, OH, (un)substituted alkoxy or aryloxy, NH₂ or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH₂ or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R₁-R₈ = H, halo, NO₂, cyano, OH or derivs., NH₂ or derivs., acyl, SH or derivs., etc.; R₉ = H, OH, (un)substituted alkoxy, aryloxy, NH₂ or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prep'd. by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepn's. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepn's. given), carried out in refluxing ClCH₂CH₂Cl in the presence of SnCl₄, gave the invention quinolinone III. Many compds. I and II had in vitro IC₅₀ values of less than 10 .mu.M with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

IT 405168-52-7P, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-

10/613,411

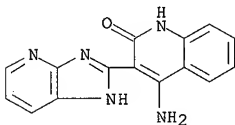
2(1H)-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

RN 405168-52-7 CA

CN 2(1H)-Quinolinone, 4-amino-3-(1H-imidazo[4,5-b]pyridin-2-yl)- (9CI) (CA INDEX NAME)



IT 405168-52-7P, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-53-8P, 4-Amino-3-(5-(morpholin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-54-9P, 4-Amino-5-((2R,6S)-2,6-dimethylmorpholin-4-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-55-0P, 4-Amino-3-[5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-25-7P, 4-Amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-26-8P, 4-Amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-79-1P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-83-7P, 6-(3-Acetylphenyl)-4-[[{(3R)-1-azabicyclo[2.2.2]oct-3-yl]amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-85-9P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7-(morpholin-4-yl)quinolin-2(1H)-one 405169-87-1P, N-[3-[4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl]-2-oxo-1,2-dihydroquinolin-6-yl]phenyl]acetamide 405169-89-3P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-6-fluoro-7-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-92-8P, 6-Chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-96-2P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(trifluoromethyl)phenyl]quinolin-2(1H)-one 405169-97-3P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one 405170-02-7P, 4-[[{(3R)-1-Azabicyclo[2.2.2]oct-3-yl]amino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405170-06-1P, 4-Hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; prepn. of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

L6 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 136:263158 CA

TITLE: Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular

10/613,411

endothelial growth factor receptor tyrosine kinase,
and useful as anticancer agents

INVENTOR(S): Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim;
Shafer, Cynthia; Taylor, Clarke; McCrea, Bill;
McBride, Chris; Jazan, Elisa; Wernette-Hammond,
Mary-Ellen; Harris, Alex

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

Bad Date

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022598	A1	20020321	WO 2001-US42131	20010911
WO 2002022598	C1	20021121		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2001093275	A5	20020326	AU 2001-93275	20010911
EP 1317442	A1	20030611	EP 2001-973722	20010911
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
NO 2003001097	A	20030325	NO 2003-1097	20030310
PRIORITY APPLN. INFO.:			US 2000-232159P P	20000911
			WO 2001-US42131 W	20010911
OTHER SOURCE(S):		MARPAT 136:263158		
GI				

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patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepn. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepn. given), carried out in refluxing ClCH₂CH₂Cl in the presence of SnCl₄, gave the invention quinolinone III. Many compds. I and II had in vitro IC₅₀ values of less than 10 .mu.M with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

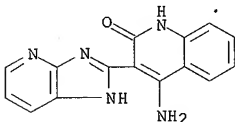
IT 405168-52-7P, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

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RN 405168-52-7 CA

CN 2(1H)-Quinolinone, 4-amino-3-(1H-imidazo[4,5-b]pyridin-2-yl)- (9CI) (CA INDEX NAME)



IT 405168-52-7P, 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-53-8P, 4-Amino-3-(5-(morpholin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-54-9P, 4-Amino-5-((2R,6S)-2,6-dimethylmorpholin-4-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405168-55-0P, 4-Amino-3-[5-(3-(dimethylamino)pyrrolidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-25-7P, 4-Amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-26-8P, 4-Amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one 405169-79-1P, 4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-83-7P, 6-(3-Acetylphenyl)-4-[[((3R)-1-azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-85-9P, 4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7-(morpholin-4-yl)quinolin-2(1H)-one 405169-87-1P, N-[3-[4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl]acetamide 405169-89-3P, 4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-6-fluoro-7-(1H-imidazol-1-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-92-8P, 6-Chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one 405169-96-2P, 4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-(2-(trifluoromethyl)phenyl)quinolin-2(1H)-one 405169-97-3P, 4-[[((3R)-1-Azabicyclo[2.2.2]oct-3-yl)amino]-3-(3H-imidazo[4,5-b]pyridin-2-

yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one 405170-02-7P,
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 4-Hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; prepn. of benzimidazolyl-substituted quinolinone
 derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer
 agents)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 110:154319 CA

TITLE: Preparation of 6-heterocyclylcarbostyryl derivatives
 for treatment of heart diseases

INVENTOR(S): Tamada, Shigeharu; Fujioka, Takafumi; Ogawa, Hidenori;
 Teramoto, Shuji; Kondo, Kazumi

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 30 pp.

CODEN: JKXXAF

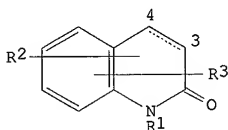
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

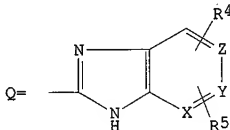
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63230687	A2	19880927	JP 1987-65202	19870318
JP 07121937	B4	19951225		
PRIORITY APPLN. INFO.: MARPAT 110:154319			JP 1987-65202	19870318
OTHER SOURCE(S):				
GI				



I



AB The title compds. [I, R1 = H, lower alkyl, lower alkenyl, phenyl-lower alkyl; R2 = Q (wherein X, Y, Z = CH or N, R4, R5 = H, lower alkoxy, halo, or NH2); R3 = H, halo, NO2, NH2, lower alkanoylamino, lower alkoxy, OH, lower alkyl, lower alkylthio, satd. 5- or 6-membered (lower alkyl) heterocyclyl, 5- or 6-membered heterocyclyl-lower alkyl; the linkage between 3- and 4-position is a single or double bond] were prepd. as cardiotonics, etc. 7-Methoxy-6-carboxy-3,4-dihydrocarbostyryl 0.3 and 3,4-diaminopyridine 0.16 g were added to a 1:10 mixt. of P205 and Me2SO3H. The mixt. was heated 2 h at 100.degree., poured into ice-water, and made weakly alk. with 10% aq. NaOH and satd. NaHCO3. The pptd. crystals were removal by filtration, washed with H2O, dried and purified on a silica gel chromatog. to give, after acidification with HCl in EtOH, 0.29 g

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7-methoxy-6-[1H-imidazo[4,5-c]pyridin-2-yl]-3,4-dihydrocarbostyryl (II)-HCl.H₂O. II.HCl.H₂O at 300 n mol increased myocardial contractility 23.1% and coronary blood flow 0.4 mL/min in dog heart in vitro. 1 ML ampules were formulated from II 500, polyethyleneglycol 0.3, NaCl 0.9, polyoxyethylenesorbitan monooleate 0.4, sodium metabisulfite 0.1, methylparaben 0.18, propylparaben 0.02 g, and water 100 mL.

IT 119714-56-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiotonic)

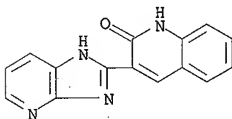
RN 119714-56-6 CA

CN 2(1H)-Quinolinone, 3-(1H-imidazo[4,5-b]pyridin-2-yl)-, ethanedioate (2:1) (9CI) (CA INDEX NAME)

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CRN 119714-55-5

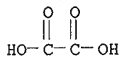
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CM 2

CRN 144-62-7

CMF C2 H2 O4



IT 119714-56-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiotonic)

=> d his

(FILE 'HOME' ENTERED AT 13:56:25 ON 05 JAN 2004)

FILE 'REGISTRY' ENTERED AT 13:56:31 ON 05 JAN 2004

L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 327 S L1 FULL
L4 309 S L2 FULL
L5 18 S L3 NOT L4

FILE 'CA' ENTERED AT 13:57:15 ON 05 JAN 2004

L6 3 S L5

10/613,411

---Logging off of STN---

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 13:57:48 ON 05 JAN 2004